

## PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner  
US Department of Commerce  
United States Patent and Trademark  
Office, PCT  
2011 South Clark Place Room  
CP2/5C24  
Arlington, VA 22202  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 03 July 2001 (03.07.01)	
International application No. PCT/EP00/08487	Applicant's or agent's file reference PU3517
International filing date (day/month/year) 31 August 2000 (31.08.00)	Priority date (day/month/year) 04 September 1999 (04.09.99)
Applicant PIANETTI, Pascal, Maurice, Charles et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

23 March 2001 (23.03.01)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Zakaria EL KHODARY

Telephone No.: (41-22) 338.83.38

## PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

To:

CRAWLEY, Karen  
GlaxoSmithKline  
Corporate Intellectual Property  
Two New Horizons Court  
Brentford  
Middlesex TW8 9EP  
ROYAUME-UNIDate of mailing (day/month/year)  
13 juillet 2001 (13.07.01)Applicant's or agent's file reference  
PU3517

## IMPORTANT NOTIFICATION

International application No.  
PCT/EP00/08487International filing date (day/month/year)  
31 août 2000 (31.08.00)

## 1. The following indications appeared on record concerning:

☐ the applicant ☐ the inventor ☒ the agent ☐ the common representative

## Name and Address

CRAWLEY, Karen  
Glaxo Wellcome plc  
Berkeley Avenue  
Greenford, Middlesex UB6 0NN  
United Kingdom

State of Nationality

State of Residence

Telephone No.

020 8966 8000

Facsimile No.

020 8966 8838

Teleprinter No.

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☐ the name ☒ the address ☐ the nationality ☐ the residence

## Name and Address

CRAWLEY, Karen  
GlaxoSmithKline  
Corporate Intellectual Property  
Two New Horizons Court  
Brentford  
Middlesex TW8 9EP  
United Kingdom

State of Nationality

State of Residence

Telephone No.

020 8966 8412

Facsimile No.

020 8966 8838

Teleprinter No.

## 3. Further observations, if necessary:

## 4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned  
☐ the International Searching Authority ☒ the elected Offices concerned  
☒ the International Preliminary Examining Authority ☐ other:The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Authorized officer

Christine Carrié

Facsimile No.: (41-22) 740.14.35

Telephone No.: (41-22) 338.83.38

## TENT COOPERATION TREA

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

CRAWLEY, Karen  
GlaxoSmithKline  
Corporate Intellectual Property  
(CN9.25.1)  
980 Great West Road  
Brentford  
Middlesex TW8 9GS  
ROYAUME-UNI

Date of mailing (day/month/year)

14 February 2002 (14.02.02)

Applicant's or agent's file reference

PU3517

## IMPORTANT NOTIFICATION

International application No.

PCT/EP00/08487

International filing date (day/month/year)

31 August 2000 (31.08.00)

## 1. The following indications appeared on record concerning:

☐ the applicant ☐ the inventor ☒ the agent ☐ the common representative

Name and Address

CRAWLEY, Karen  
GlaxoSmithKline  
Corporate Intellectual Property  
Two New Horizons Court  
Brentford  
Middlesex TW8 9EP  
United Kingdom

State of Nationality

State of Residence

Telephone No.

020 8966 8412

Facsimile No.

020 8966 8838

Teleprinter No.

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☐ the name ☒ the address ☐ the nationality ☐ the residence

Name and Address

CRAWLEY, Karen  
GlaxoSmithKline  
Corporate Intellectual Property  
(CN9.25.1)  
980 Great West Road  
Brentford  
Middlesex TW8 9GS  
United Kingdom

State of Nationality

State of Residence

Telephone No.

44 20 8047 5000

Facsimile No.

44 20 8047 6894

Teleprinter No.

## 3. Further observations, if necessary:

## 4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned  
☐ the International Searching Authority ☒ the elected Offices concerned  
☐ the International Preliminary Examining Authority ☐ other:The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Authorized officer

Sean Taylor

Facsimile No.: (41-22) 740.14.35

Telephone No.: (41-22) 338.83.38

## PATENT COOPERATION TREATY

10/070084

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

CRAWLEY, Karen  
GlaxoSmithKline  
Corporate Intellectual Property  
(CN9.25.1)  
980 Great West Road  
Brentford  
Middlesex TW8 9GS  
United Kingdom

RECEIVED  
FEB 12 2003  
TECH CENTER 1600/2900

Date of mailing (day/month/year) 10 décembre 2002 (10.12.02)	<b>IMPORTANT NOTIFICATION</b>
Applicant's or agent's file reference PU3517	
International application No. PCT/EP00/08487	International filing date (day/month/year) 31 août 2000 (31.08.00)

1. The following indications appeared on record concerning: <input checked="" type="checkbox"/> the applicant <input checked="" type="checkbox"/> the inventor <input type="checkbox"/> the agent <input type="checkbox"/> the common representative		
Name and Address PIANETTI, Pascal, Maurice, Charles	State of Nationality FR	State of Residence FR
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning: <input checked="" type="checkbox"/> the person <input type="checkbox"/> the name <input checked="" type="checkbox"/> the address <input type="checkbox"/> the nationality <input type="checkbox"/> the residence		
Name and Address PIANETTI, Pascal, Maurice, Charles Laboratoire GlaxoSmithKline Centre de Recherches Z.A. de Couraboeuf 25, Avenue de Québec F-91940 Les Ulis France	State of Nationality FR	State of Residence FR
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary: <b>Corrected version of IB/306 mailed on 26 March 2002. The person in box No. 2 will be the applicant/inventor for US only.</b>		
4. A copy of this notification has been sent to: <input checked="" type="checkbox"/> the receiving Office <input type="checkbox"/> the designated Offices concerned <input type="checkbox"/> the International Searching Authority <input checked="" type="checkbox"/> the elected Offices concerned <input checked="" type="checkbox"/> the International Preliminary Examining Authority <input type="checkbox"/> other:		

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	Authorized officer Ki-Nam HA  Telephone No.: (41-22) 338.83.38
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## PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

CRAWLEY, Karen  
GlaxoSmithKline  
Corporate Intellectual Property  
(CN9.25.1)  
980 Great West Road  
Brentford  
Middlesex TW8 9GS  
ROYAUME-UNI

Date of mailing (day/month/year)  
26 March 2002 (26.03.02)

Applicant's or agent's file reference  
PU3517

International application No.  
PCT/EP00/08487

## IMPORTANT NOTIFICATION

International filing date (day/month/year)  
31 August 2000 (31.08.00)

## 1. The following indications appeared on record concerning:

☒ the applicant ☐ the inventor ☐ the agent ☐ the common representative

## Name and Address

PIANETTI, Pascal, Maurice, Charles  
Laboratoire Glaxo Wellcome  
Centre de Recherches  
25, avenue de Québec  
F-91951 Les Ulis  
France

State of Nationality  
FR

State of Residence  
FR

Telephone No.

Facsimile No.

Teleprinter No.

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☒ the person ☐ the name ☐ the address ☐ the nationality ☐ the residence

## Name and Address

PIANETTI, Pascal, Maurice, Charles  
Laboratoire Glaxo Wellcome  
Centre de Recherches  
25, avenue de Québec  
F-91951 Les Ulis  
France

State of Nationality  
FR

State of Residence  
FR

Telephone No.

Facsimile No.

Teleprinter No.

## 3. Further observations, if necessary:

The person in box No. 2 will be the applicant for all designated States except US.

## 4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned  
☐ the International Searching Authority ☒ the elected Offices concerned  
☐ the International Preliminary Examining Authority ☐ other:

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Ki-Nam HA

Telephone No.: (41-22) 338.83.38

## TENT COOPERATION TREA

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

CRAWLEY, Karen  
Glaxo Wellcome plc  
Berkeley Avenue  
Greenford, Middlesex UB6 0NN  
ROYAUME-UNI

Date of mailing (day/month/year) 13 March 2001 (13.03.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference PU3517	
International application No. PCT/EP00/08487	International filing date (day/month/year) 31 August 2000 (31.08.00)

1. The following indications appeared on record concerning:

☒ the applicant ☒ the inventor ☐ the agent ☐ the common representative

Name and Address PIANETTI, Pascal, Maurice, Charles Laboratoire Glaxo Wellcome Centre de Recherches Z.A. de Couraboeuf 25, avenue de Québec F-91940 Les Ulis France	State of Nationality FR	State of Residence FR
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☒ the person ☐ the name ☐ the address ☐ the nationality ☐ the residence

Name and Address PIANETTI, Pascal, Maurice, Charles Laboratoire Glaxo Wellcome Centre de Recherches 25, avenue de Québec F-91951 Les Ulis France	State of Nationality FR	State of Residence FR
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:  
**The Applicant's status has been changed into applicant/inventor for the US only.**

4. A copy of this notification has been sent to:

☒ the receiving Office ☒ the designated Offices concerned  
☐ the International Searching Authority ☐ the elected Offices concerned  
☐ the International Preliminary Examining Authority ☐ other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Eugénia Santos Telephone No.: (41-22) 338.83.38
---	--

1070084(56107)

Copy for the Elected Office (EO/US)

PCT/EP00/08487

## PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

CRAWLEY, Karen  
GlaxoSmithKline  
Corporate Intellectual Property  
(CN9.25.1)  
980 Great West Road  
Brentford  
Middlesex TW8 9GS  
ROYAUME-UNI

Date of mailing (day/month/year) 19 April 2002 (19.04.02)	<b>IMPORTANT NOTIFICATION</b>
Applicant's or agent's file reference PU3517	
International application No. PCT/EP00/08487	International filing date (day/month/year) 31 August 2000 (31.08.00)

## 1. The following indications appeared on record concerning:

☒ the applicant ☐ the inventor ☐ the agent ☐ the common representative

Name and Address PIANETTI, Pascal, Maurice, Charles Laboratoire Glaxo Wellcome Centre de Recherches 25, avenue de Québec F-91951 Les Ulis France	State of Nationality FR	State of Residence FR
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☐ the name ☒ the address ☐ the nationality ☐ the residence

Name and Address PIANETTI, Pascal, Maurice, Charles Laboratoire GlaxoSmithKline Centre de Recherches Z.A. de Couraboeuf 25, Avenue de Québec F-91940 Les Ulis France	State of Nationality FR	State of Residence FR
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

## 3. Further observations, if necessary:

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<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned
<input type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Kiwa MPAY Telephone No.: (41-22) 338.83.38
---	---

# INTERNATIONAL SEARCH REPORT

Intern. Application No.  
PCT/EP 00/08487

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D277/24 A61K31/16 A61K31/33 A61P31/00 C07D417/12  
C07D307/80 C07D333/56 C07D207/32 C07D409/04 C07D279/34  
C07C311/46 C07D233/22 C07D295/08 C07D277/62 C07D209/48

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D C07C A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, BEILSTEIN Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	P G WYATT ET AL: "JOURNAL OF MEDICINAL CHEMISTRY, US, AMERICAN CHEMICAL SOCIETY. WASHINGTON" JOURNAL OF MEDICINAL CHEMISTRY, US, AMERICAN CHEMICAL SOCIETY. WASHINGTON, vol. 38, no. 10, 1995, pages 1657-1665, XP002084134 ISSN: 0022-2623 page 1658; table 1 page 1659; table 2 page 1660; table 3	1-37
P, X	WO 99 55682 A (UNIV GEORGETOWN) 4 November 1999 (1999-11-04) figure 10	1
	-/-	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

6 February 2001

Date of mailing of the international search report

21/02/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Pauwels, G



# INTERNATIONAL SEARCH REPORT

Interr. Application No  
PCT/EP 00/08487

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D277/64 C07D275/04 C07D233/84 C07D277/36 C07D277/28  
C07D263/32 C07C317/40 C07D521/00 C07D285/06 C07D231/56  
C07D409/12 C07D333/22 C07D241/44 C07D213/50 C07D235/28

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FR 1 552 793 A (ETS. CLYN-BILA) 10 January 1969 (1969-01-10) page 6; example 56	1
X	US 4 883 815 A (ASCHWENDEN WERNER ET AL) 28 November 1989 (1989-11-28) example 27	1
X	US 4 207 234 A (HASHIMOTO MASASHI ET AL) 10 June 1980 (1980-06-10) example 190	1
X	SUGASAWA, TSUTOMU ET AL: "1-Azacycloalkyl-1,4-benzodiazepin-2-ones with antianxiety- antidepressant actions" J. MED. CHEM. (1985), 28(6), 699-707 , XP002159556 page 700; figure 15	1
	-/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
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- \*Y\* document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*G\* document member of the same patent family

Date of the actual completion of the international search

6 February 2001

Date of mailing of the international search report

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Pauwels, G

# INTERNATIONAL SEARCH REPORT

Intern. Application No  
PCT/EP 00/08487

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D235/06 C07D235/26 C07D209/08 C07C259/06 C07C235/24  
C07D295/12 C07D249/18 C07D233/54 C07D333/38 C07D213/61  
C07D401/12 C07C323/22 C07C317/24 C07C311/24 C07D213/64

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CAPUANO, LILLY ET AL: "Darstellung von alpha-'2- alkoxy-carbonyl-anilino!- und alpha-'2-Acylanilino!-carbonsäureamiden" JUSTUS LIEBIGS ANN: CHEM. (1968), 712, 73-8, XP002159557 page 73; figure 4J page 78, paragraph 1	1
X	BRANDL, E.: "Penicillin reactions. 1. Behavior towards penicillinase" SCI. PHARM. (1971), 39(4), 267-92 , XP000979965 page 279; example 95	1

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

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\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*Z\* document member of the same patent family

Date of the actual completion of the international search

6 February 2001

Date of mailing of the international search report

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax (+31-70) 340-3016

Authorized officer

Pauwels, G

# INTERNATIONAL SEARCH REPORT

Interr. Application No

PCT/EP 00/08487

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D333/72 C07D215/08 C07D217/06 C07D213/75 C07D261/16  
 C07C311/08 C07D211/44 C07D407/12 C07D307/46 C07D333/54  
 C07D213/42 C07D333/20 C07D207/09 C07D307/14 C07D207/20

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*8\* document member of the same patent family

Date of the actual completion of the international search

6 February 2001

Date of mailing of the international search report

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel (+31-70) 340-2040, Tx. 31 651 epo nl  
 Fax (+31-70) 340-3016

Authorized officer

Pauwels, G

# INTERNATIONAL SEARCH REPORT

Intern. Application No

PCT/EP 00/08487

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D213/85 C07D213/84 C07D333/32 C07C255/56 C07C275/10  
C07D295/22 C07C255/44 C07D295/14 C07C237/42

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

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- \*O\* document referring to an oral disclosure, use, exhibition or other means
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- \*Y\* document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*A\* document member of the same patent family

Date of the actual completion of the international search

6 February 2001

Date of mailing of the international search report

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax (+31-70) 340-3016

Authorized officer

Pauwels, G

# INTERNATIONAL SEARCH REPORT

information on patent family members

Interr. application No

PCT/EP 00/08487

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9955682 A	04-11-1999	AU 3669199 A	16-11-1999
FR 1552793 A	10-01-1969	DE 1643317 A	16-06-1971
		GB 1197597 A	08-07-1970
		US 3551478 A	29-12-1970
US 4883815 A	28-11-1989	AU 603470 B	15-11-1990
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		DD 277071 A	21-03-1990
		DK 405888 A	22-01-1989
		EP 0300371 A	25-01-1989
		FI 883441 A	22-01-1989
		GB 2207135 A, B	25-01-1989
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		IN 167395 A	20-10-1990
		JP 1047748 A	22-02-1989
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		ZA 8805102 A	29-03-1989
		ZW 9288 A	01-02-1989
US 4207234 A	10-06-1980	US 4472300 A	18-09-1984

## PATENT COOPERATION TREATY

23 MAR 2001

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

CRAWLEY, Karen  
Glaxo Wellcome plc  
Berkeley Avenue  
Greenford, Middlesex UB6 0NN  
ROYAUME-UNIDate of mailing (day/month/year)  
13 March 2001 (13.03.01)Applicant's or agent's file reference  
PU3517International application No.  
PCT/EP00/08487

## IMPORTANT NOTIFICATION

International filing date (day/month/year)  
31 August 2000 (31.08.00)

1. The following indications appeared on record concerning:

☒ the applicant ☒ the inventor ☐ the agent ☐ the common representative

Name and Address

PIANETTI, Pascal, Maurice, Charles  
Laboratoire Glaxo Wellcome  
Centre de Recherches  
Z.A. de Couraboëuf  
25, avenue de Québec  
F-91940 Les Ulis  
FranceState of Nationality  
FRState of Residence  
FR

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☒ the person ☐ the name ☐ the address ☐ the nationality ☐ the residence

Name and Address

PIANETTI, Pascal, Maurice, Charles  
Laboratoire Glaxo Wellcome  
Centre de Recherches  
25, avenue de Québec  
F-91951 Les Ulis  
FranceState of Nationality  
FRState of Residence  
FR

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

The Applicant's status has been changed into applicant/inventor for the US only.

4. A copy of this notification has been sent to:

☒ the receiving Office  
☐ the International Searching Authority  
☐ the International Preliminary Examining Authority☒ the designated Offices concerned  
☐ the elected Offices concerned  
☐ other:The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Authorized officer

Eugénia Santos

Facsimile No.: (41-22) 740.14.35  
Form PCT/IB/306 (March 1994)

Telephone No.: (41-22) 338.83.38

003893607

## PATENT COOPERATION TREATY

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23 JUL 2001

NEW HORIZONS

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

CRAWLEY, Karen  
GlaxoSmithKline  
Corporate Intellectual Property  
Two New Horizons Court  
Brentford  
Middlesex TW8 9EP  
ROYAUME-UNIDate of mailing (day/month/year)  
13 July 2001 (13.07.01)Applicant's or agent's file reference  
PU3517International application No.  
PCT/EP00/08487International filing date (day/month/year)  
31 August 2000 (31.08.00)

## IMPORTANT NOTIFICATION

## 1. The following indications appeared on record concerning:

☐ the applicant ☐ the inventor ☒ the agent ☐ the common representative

## Name and Address

CRAWLEY, Karen  
Glaxo Wellcome plc  
Berkeley Avenue  
Greenford, Middlesex UB6 0NN  
United Kingdom

## Corporate Intellectual Property

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B6 0NN

24 JUL 2001

INIT

Action  
DateATTN  
VCEFILE  
BKC

State of Nationality

State of Residence

Telephone No.

020 8966 8000

Facsimile No.

020 8966 8838

Teleprinter No.

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☐ the name ☒ the address ☐ the nationality ☐ the residence

## Name and Address

CRAWLEY, Karen  
GlaxoSmithKline  
Corporate Intellectual Property  
Two New Horizons Court  
Brentford  
Middlesex TW8 9EP  
United Kingdom

State of Nationality

State of Residence

Telephone No.

020 8966 8412

Facsimile No.

020 8966 8838

Teleprinter No.

## 3. Further observations, if necessary:

## 4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned  
☐ the International Searching Authority ☒ the elected Offices concerned  
☒ the International Preliminary Examining Authority ☐ other:The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Authorized officer

C. CARRIE  
Christine Carrié

Facsimile No.: (41-22) 740.14.35

Telephone No.: (41-22) 338.83.38

101070084

**PCT REQUEST**

1/5

Original (for SUBMISSION) - printed on 15.08.2000 04:08:03 PM

PU3517

0 0-1	For receiving Office use only International Application No.	<b>PCT/EP 00 / 08487</b>
0-2	International Filing Date	<b>31 AUG 2000</b> — <b>(31 08. 2000)</b>
0-3	Name of receiving Office and "PCT International Application"	<b>EUROPEAN PATENT OFFICE PCT INTERNATIONAL APPLICATION</b>
0-4 0-4-1	Form - PCT/RO/101 PCT Request Prepared using	<b>PCT-EASY Version 2.91 (updated 01.07.2000)</b>
0-5	<b>Petition</b> The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty	
0-6	Receiving Office (specified by the applicant)	<b>European Patent Office (EPO) (RO/EP)</b>
0-7	Applicant's or agent's file reference	<b>PU3517</b>
I	Title of Invention	<b>BENZOPHENONES AS INHIBITORS OF REVERSE TRANSCRIPTASE</b>
II	Applicant	
II-1	This person is:	<b>applicant only</b>
II-2	Applicant for	<b>all designated States except US</b>
II-4	Name	<b>GLAXO GROUP LIMITED</b>
II-5	Address:	<b>Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom</b>
II-6	State of nationality	<b>GB</b>
II-7	State of residence	<b>GB</b>
II-8	Telephone No.	<b>020 8966 8000</b>
II-9	Facsimile No.	<b>020 8966 8838</b>
III-1	Applicant and/or inventor	
III-1-1	This person is:	<b>applicant and inventor</b>
III-1-2	Applicant for	<b>US only</b>
III-1-4	Name (LAST, First)	<b>ANDREWS, Clarence, Webster</b>
III-1-5	Address:	<b>Glaxo Wellcome Inc. Five Moore Drive Research Triangle Park, NC NC 27709 United States of America</b>
III-1-6	State of nationality	<b>US</b>
III-1-7	State of residence	<b>US</b>



## PCT REQUEST

2/5

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PU3517

III-2	Applicant and/or inventor	applicant and inventor US only CHAN, Joseph, Howing Glaxo Wellcome Inc Five Moore Drive Research Triangle Park, NC NC 27709 United States of America
III-2-1	This person is:	
III-2-2	Applicant for	
III-2-4	Name (LAST, First)	
III-2-5	Address:	
III-2-6	State of nationality	US
III-2-7	State of residence	US
III-3	Applicant and/or inventor	applicant and inventor US only FREEMAN, George, Andrew Glaxo Wellcome Inc. Five Moore Drive Research Triangle Park, NC NC 27709 United States of America
III-3-1	This person is:	
III-3-2	Applicant for	
III-3-4	Name (LAST, First)	
III-3-5	Address:	
III-3-6	State of nationality	US
III-3-7	State of residence	US
III-4	Applicant and/or inventor	applicant only all designated States except US PIANETTI, Pascal, Maurice, Charles Laboratoire Glaxo Wellcome Centre de Recherches Z.A. de Couraboeuf F-91940 Les Ulis 25 avenue de Quebec France
III-4-1	This person is:	
III-4-2	Applicant for	
III-4-4	Name (LAST, First)	
III-4-5	Address:	
III-4-6	State of nationality	FR
III-4-7	State of residence	FR
III-5	Applicant and/or inventor	applicant and inventor US-only ROMINES, Karen, Rene Glaxo Wellcome Inc Five Moore Drive Research Triangle Park, NC NC 27709 United States of America
III-5-1	This person is:	
III-5-2	Applicant for	
III-5-4	Name (LAST, First)	
III-5-5	Address:	
III-5-6	State of nationality	US
III-5-7	State of residence	US

## PCT REQUEST

3/5

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PU3517

III-6	Applicant and/or inventor	
III-6-1	This person is:	applicant and inventor
III-6-2	Applicant for	US only
III-6-4	Name (LAST, First)	TIDWELL, Jeffrey, H.
III-6-5	Address:	Glaxo Wellcome Inc. Five Moore Drive Research Triangle Park, NC NC 27709 United States of America
III-6-6	State of nationality	US
III-6-7	State of residence	US
III-7	Applicant and/or inventor	
III-7-1	This person is:	applicant only
III-7-2	Applicant for	all designated States except US
III-7-4	Name (LAST, First)	PIANETTI, Pascal, Maurice, Charles
III-7-5	Address:	Laboratoire Glaxo Wellcome Centre de Recherches Z.A. de Couraboeuf F-91940 Les Ulis 25 avenue de Quebec France
III-7-6	State of nationality	FR
III-7-7	State of residence	FR
IV-1	Agent or common representative; or address for correspondence The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:	agent
IV-1-1	Name (LAST, First)	CRAWLEY, Karen
IV-1-2	Address:	Glaxo Wellcome Plc Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom
IV-1-3	Telephone No.	020 8966 8000
IV-1-4	Facsimile No.	020 8966 8838

## PCT REQUEST

4/5

Original (for SUBMISSION) - printed on 15.08.2000 04:08:03 PM

PU3517

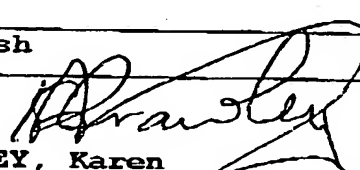
V	<b>Designation of States</b>	
V-1	Regional Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	<p>AP: GH GM KE LS MW MZ SD SL SZ TZ UG ZW and any other State which is a Contracting State of the Harare Protocol and of the PCT</p> <p>EA: AM AZ BY KG KZ MD RU TJ TM and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT</p> <p>EP: AT BE CH&amp;LI CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE and any other State which is a Contracting State of the European Patent Convention and of the PCT</p> <p>OA: BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG and any other State which is a member State of OAPI and a Contracting State of the PCT</p>
V-2	National Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	<p>AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH&amp;LI CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW</p>
V-5	<b>Precautionary Designation Statement</b> In addition to the designations made under items V-1, V-2 and V-3, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except any designation(s) of the State(s) indicated under item V-6 below. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit.	
V-6	<b>Exclusion(s) from precautionary designations</b>	NONE
VI-1	<b>Priority claim of earlier national application</b>	
VI-1-1	Filing date	04 September 1999 (04.09.1999)
VI-1-2	Number	9920872.0
VI-1-3	Country	GB
VII-1	<b>International Searching Authority Chosen</b>	European Patent Office (EPO) (ISA/EP)

## PCT REQUEST

5/5

Original (for SUBMISSION) - printed on 15.08.2000 04:08:03 PM

PU3517

VIII	Check list		
VIII-1	Request	5	number of sheets
VIII-2	Description	403	electronic file(s) attached
VIII-3	Claims	26	-
VIII-4	Abstract	1	-
VIII-5	Drawings	0	pu3517_abstract.txt
VIII-7	TOTAL	435	-
VIII-8	Accompanying items		paper document(s) attached
VIII-9	Fee calculation sheet		electronic file(s) attached
VIII-16	Separate signed power of attorney		-
VIII-16	PCT-EASY diskette	-	-
VIII-18	Figure of the drawings which should accompany the abstract		diskette
VIII-19	Language of filing of the international application	English	
IX-1	Signature of applicant or agent		
IX-1-1	Name (LAST, First)	CRAWLEY, Karen	

## FOR RECEIVING OFFICE USE ONLY

10-1	Date of actual receipt of the purported international application	31 AUG 2000	(31 08. 2000)
10-2	Drawings:		
10-2-1	Received		
10-2-2	Not received		
10-3	Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application		
10-4	Date of timely receipt of the required corrections under PCT Article 11(2)		
10-5	International Searching Authority	ISA/EP	
10-6	Transmittal of search copy delayed until search fee is paid		

## FOR INTERNATIONAL BUREAU USE ONLY

11-1	Date of receipt of the record copy by the International Bureau	
------	--	--

REC'D 27 NOV 2001

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference PU3517	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP00/08487	International filing date (day/month/year) 31/08/2000	Priority date (day/month/year) 04/09/1999
International Patent Classification (IPC) or national classification and IPC C07D277/24		
Applicant GLAXO GROUP LIMITED et al.		

- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 7 sheets, including this cover sheet.  
  
☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand  23/03/2001	Date of completion of this report  22.11.2001
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Usuelli, A  Telephone No. +49 89 2399 7366  

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP00/08487

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17):*)  
**Description, pages:**

1-403 as originally filed

**Claims, No.:**

1-37 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/08487

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

## III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 27-30 (industrial applicability).

because:

- ☒ the said international application, or the said claims Nos. 27-30 relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos.:

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 2-7, 9-37
	No: Claims 1, 8
Inventive step (IS)	Yes: Claims
	No: Claims 1-37
Industrial applicability (IA)	Yes: Claims 1-26, 31-37

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP00/08487

No: Claims

2. Citations and explanations  
see separate sheet



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP00/08487

**Re Item III**

**Non-establishment of opinion**

Claims 27-30 relate to subject matter considered by this Authority to be covered by the provisions of Rule 67.1 (iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of this claim, cf. Article 34(4)(a)(i) PCT.

**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1- In the present Written Opinion reference is made to the following documents:

d1: J. MED. CHEM. vol. 38, no. 10, 1995, pages 1657-1665,

d2: FR 1 552 793 A

d3: US 4 883 815 A

d4: US 4 207 234 A

d5: J. MED. CHEM. (1985), 28(6), pages 699-707.

d6: JUSTUS LIEBIGS ANN. CHEM. (1968), 712, pages 73-8

d7: SCI. PHARM. (1971), 39(4), pages 267-92

**2- Novelty**

2.1- The compound of formula 15 disclosed in scheme II of d5, in which X=4-NO<sub>2</sub> and Y=2-Cl (cf. page 700 Method B, in conjunction with page 699, line 8 of paragraph "Chemistry"), is encompassed by present claims 1 and 8. The compound 15 in which X=Cl and Y=2-F, is excluded from these claims for the effect of the disclaimers. Accordingly, claims 1 and 8 do not comply with requirements of Art. 33(2) PCT.

2.2- Some compounds disclosed in d1, d2, d4, d6 and d7 contain a benzoyl group and an amide moiety attached by a linking group. These compounds differ from the compounds of the present application in that the groups attached to the nitrogen of the amide radical differ from the present groups R<sub>3</sub>/R<sub>4</sub>.

Compounds of d3 differ from the present compounds in that they lack the moiety -COR<sub>1</sub>.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP00/08487

**3- Inventive step**

3.1- D1 discloses a class of benzophenone derivatives acting as inhibitors of HIV-1 reverse transcriptase. This document is regarded as the closest state of the art. The technical problem can be seen in the provision of further inhibitors of HIV reverse transcriptase.

Said problem has been allegedly solved by present compounds of formulae (I) and (IV) (compounds of formulae IA, IB, IC, ID, II and III appear encompassed by formula I). For the purpose of assessing the inventive step during the International Preliminary Examination it is assumed that these compounds indeed act as HIV inhibitors, i.e. solve the above defined technical problem.

3.2- The compounds of Tables 1 and 2 of d1 differ from the compounds of the invention only for the nature of the group R attached to the phenyl ring of the aniline moiety. In the compounds of formula 1a-1l said R group is a radical of formula  $-\text{O}(\text{CH}_2)_2\text{NEt}_2$  or a hydrogen. In the corresponding position the compounds of the invention can be substituted, for instance, by a  $\text{C}_1$ - $\text{C}_8$ alkylamino radical or by small group such as hydroxy and halogen.

Due to this structural similarity with the HIV-inhibitors disclosed in d1, it appears that the skilled person would have expected similar properties also from the present compounds.

Thus, the presence of an inventive step should be demonstrated preferably by means of comparative tests, e.g. by showing a quantitative superiority or unexpected effects vis-à-vis the closest prior art.

It is observed that the Applicant indicates in the present description (page 1 lines 30-33) that the compounds of d1 induce "resistance virus and were inactive against a common resistance strain". Considering the close similarity between the compounds of the invention and the compound of d1 and the broad scope of the formulae (I) and (IV), it should be credible from the comparative tests that any advantage over the compounds of d1 is provided by substantially all the claimed compounds.

The above considerations apply also to those compounds containing an heterocyclic moiety instead of a phenyl ring (i.e. compounds of claims 10-13 and 21). In fact the broad definition of heterocyclic group (cf. page 28 of the description) encompasses also rings known as bioisosters of the phenyl group.

Accordingly it appears that there are no inventive contributions in the introduction of this feature.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/EP00/08487

**4- Industrial applicability**

For the assessment of the present claims 27-30 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

## PATENT COOPERATION TREATY

cc Karen Prus 10/12/01

Corporate Intellectual Property	
RECEIVED	IN.
6 6 DEC 2001	
Agent PCT	File KE

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

CRAWLEY, Karen  
GLAXOSMITHKLINE  
Corporate Intellectual Property  
Two New Horizons Court  
Brentford  
Middlesex TW8 9EP  
GRANDE BRETAGNE

RECEIVED  
25 NOV 2001  
NEW HORIZONS COURT

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing  
(day/month/year) 22.11.2001

Applicant's or agent's file reference  
PU3517

## IMPORTANT NOTIFICATION

International application No.  
PCT/EP00/08487

International filing date (day/month/year)  
31/08/2000

Priority date (day/month/year)  
04/09/1999

Applicant  
GLAXO GROUP LIMITED et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

## 4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



European Patent Office  
D-80298 Munich  
Tel. +49 89 2399 - 0 Tx: 523656 epmu d  
Fax: +49 89 2399 - 4465

Authorized officer

Ambroa, J.R.

Tel. +49 89 2399-8012



# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>PU3517</b>	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. <b>PCT/EP00/08487</b>	International filing date (day/month/year) <b>31/08/2000</b>	Priority date (day/month/year) <b>04/09/1999</b>
International Patent Classification (IPC) or national classification and IPC <b>C07D277/24</b>		
Applicant <b>GLAXO GROUP LIMITED et al.</b>		


1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
 

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- |      |                                     |   |
|------|-------------------------------------|---|
| I    | <input checked="" type="checkbox"/> | Basis of the report   |
| II   | <input type="checkbox"/>            | Priority  |
| III  | <input checked="" type="checkbox"/> | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability  |
| IV   | <input type="checkbox"/>            | Lack of unity of invention  |
| V    | <input checked="" type="checkbox"/> | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| VI   | <input type="checkbox"/>            | Certain documents cited   |
| VII  | <input type="checkbox"/>            | Certain defects in the international application  |
| VIII | <input type="checkbox"/>            | Certain observations on the international application   |

Date of submission of the demand <b>23/03/2001</b>	Date of completion of this report <b>22.11.2001</b>
Name and mailing address of the international preliminary examining authority:  <b>European Patent Office</b> <b>D-80298 Munich</b> <b>Tel. +49 89 2399 - 0 Tx: 523656 epmu d</b> <b>Fax: +49 89 2399 - 4465</b>	Authorized officer  <b>Usuelli, A</b>  Telephone No. +49 89 2399 7366



# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/08487

## I. Basis of the report

1. With regard to the elements of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-403 as originally filed

Claims, No.:

1-37 as originally filed

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/08487

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

## III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 27-30 (industrial applicability).

because:

- ☒ the said international application, or the said claims Nos. 27-30 relate to the following subject matter which does not require an international preliminary examination (*specify*):  
see separate sheet
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 2-7, 9-37
	No: Claims 1, 8
Inventive step (IS)	Yes: Claims
	No: Claims 1-37
Industrial applicability (IA)	Yes: Claims 1-26, 31-37

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. **PCT/EP00/08487**

No: Claims

2. Citations and explanations  
see separate sheet



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP00/08487

**Re Item III**

**Non-establishment of opinion**

Claims 27-30 relate to subject matter considered by this Authority to be covered by the provisions of Rule 67.1 (iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of this claim, cf. Article 34(4)(a)(i) PCT.

**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1- In the present Written Opinion reference is made to the following documents:

d1: J. MED. CHEM. vol. 38, no. 10, 1995, pages 1657-1665,

d2: FR 1 552 793 A

d3: US 4 883 815 A

d4: US 4 207 234 A

d5: J. MED. CHEM. (1985), 28(6), pages 699-707.

d6: JUSTUS LIEBIGS ANN. CHEM. (1968), 712, pages 73-8

d7: SCI. PHARM. (1971), 39(4), pages 267-92

**2- Novelty**

2.1- The compound of formula 15 disclosed in scheme II of d5, in which X=4-NO<sub>2</sub> and Y=2-Cl (cf. page 700 Method B, in conjunction with page 699, line 8 of paragraph "Chemistry"), is encompassed by present claims 1 and 8. The compound 15 in which X=Cl and Y=2-F, is excluded from these claims for the effect of the disclaimers. Accordingly, claims 1 and 8 do not comply with requirements of Art. 33(2) PCT.

2.2- Some compounds disclosed in d1, d2, d4, d6 and d7 contain a benzoyl group and an amide moiety attached by a linking group. These compounds differ from the compounds of the present application in that the groups attached to the nitrogen of the amide radical differ from the present groups R3/R4.

Compounds of d3 differ from the present compounds in that they lack the moiety -COR1.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. **PCT/EP00/08487**

**3- Inventive step**

3.1- D1 discloses a class of benzophenone derivatives acting as inhibitors of HIV-1 reverse transcriptase. This document is regarded as the closest state of the art. The technical problem can be seen in the provision of further inhibitors of HIV reverse transcriptase.

Said problem has been allegedly solved by present compounds of formulae (I) and (IV) (compounds of formulae IA, IB, IC, ID, II and III appear encompassed by formula I). For the purpose of assessing the inventive step during the International Preliminary Examination it is assumed that these compounds indeed act as HIV inhibitors, i.e. solve the above defined technical problem.

3.2- The compounds of Tables 1 and 2 of d1 differ from the compounds of the invention only for the nature of the group R attached to the phenyl ring of the aniline moiety. In the compounds of formula 1a-1I said R group is a radical of formula  $-(CH_2)_2NEt_2$  or a hydrogen. In the corresponding position the compounds of the invention can be substituted, for instance, by a  $C_1$ - $C_6$ alkylamino radical or by small groups such as hydroxy and halogen.

Due to this structural similarity with the HIV-inhibitors disclosed in d1, it appears that the skilled person would have expected similar properties also from the present compounds.

Thus, the presence of an inventive step should be demonstrated preferably by means of comparative tests, e.g. by showing a quantitative superiority or unexpected effects vis-à-vis the closest prior art.

It is observed that the Applicant indicates in the present description (page 1 lines 30-33) that the compounds of d1 induce "resistance virus and were inactive against a common resistance strain". Considering the close similarity between the compounds of the invention and the compound of d1 and the broad scope of the formulae (I) and (IV), it should be credible from the comparative tests that any advantage over the compounds of d1 is provided by substantially all the claimed compounds.

The above considerations apply also to those compounds containing a heterocyclic moiety instead of a phenyl ring (i.e. compounds of claims 10-13 and 21). In fact the broad definition of heterocyclic group (cf. page 28 of the description) encompasses also rings known as bioisosters of the phenyl group.

Accordingly it appears that there are no inventive contributions in the introduction of this feature.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. **CT/EP00/08487**

**4- Industrial applicability**

For the assessment of the present claims 27-30 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

TO:  
PCT Examination  
International Bureau of WIPO  
34 Chimin des Colombettes  
1211 Geneva 20  
Switzerland

Fax: 011 41 22 740 1435

**Correction to PCT  
Request before  
expiration of 30th  
Month**

Applicant's File Reference  
PU3517WO

Applicant  
Glaxo Group Limited

International Application No.  
PCT/EP00/08487

International Filing Date:  
31 August 2000

30th Month Deadline:  
4 March 2002

Title: Benzophenones as Inhibitors of Reverse  
Transcriptase

**Please make the following corrections to PCT Request :**

Please change the name of inventor Clarence Webster ANDREWS to Clarence Webster ANDREWS III

Box III-1 Please change the address of inventor Clarence Webster ANDREWS, III from , Glaxo Wellcome Inc., Five Moore Drive, PO Box 13398, Research Triangle Park, NC 27709, US

Change to

GlaxoSmithKline, Five Moore Drive, PO Box 13398, Research Triangle Park, NC 27709, US

Box III-2 Please change the address of inventor Joseph Howing CHAN from Glaxo Wellcome Inc., Five Moore Drive, PO Box 13398, Research Triangle Park, NC 27709, US

Change to

GlaxoSmithKline, Five Moore Drive, PO Box 13398, Research Triangle Park, NC 27709, US

Box III-3 Please change the address of inventor George Andrew FREEMAN from Glaxo Wellcome Inc., Five Moore Drive, PO Box 13398, Research Triangle Park, NC 27709, US

Change to

GlaxoSmithKline, Five Moore Drive, PO Box 13398, Research Triangle Park, NC 27709, US

Box III-5 Please change the address of inventor Karen Rene ROMINES from Glaxo Wellcome Inc., Five Moore Drive, PO Box 13398, Research Triangle Park, NC 27709, US

Change to

GlaxoSmithKline, Five Moore Drive, PO Box 13398, Research Triangle Park, NC 27709, US

Box III-6 Please change the address of inventor Jeffrey H. TIDWELL from Glaxo Wellcome Inc., Five Moore Drive, PO Box 13398, Research Triangle Park, NC 27709, US

Change to

GlaxoSmithKline, Five Moore Drive, PO Box 13398, Research Triangle Park, NC 27709, US

Box III-7 Please change the address of inventor Pascal Maurice Charles PLANETTI from Laboratoire Glaxo Wellcome, Centre de Recherches, Z.A. de Couraboeuf, 25, avenue de Québec, F-91940 Les Ulis, France

Change to

Laboratoire GlaxoSmithKline, Centre de Recherches, Z.A. de Couraboeuf, 25, avenue de Québec, F-91940 Les Ulis, France

Please confirm receipt of this Request to Change PCT Request for 30<sup>th</sup> Month to fax 919-483-7988.

Please send PCT/IB/306 to: David J. Levy, VP, GlaxoSmithKline, Corporate Intellectual Property Department  
Five Moore Drive, PO Box 13398, Research Triangle Park, NC 27709

If there should be questions, please call (919) 483-2252.

Thank you.  
Sincerely,

*Karen L. Prus* 2/18/02  
Karen L. Prus, Agent for the Applicant

**FAXED**  
2-18-02